



Screening Diagnostics of Gestational Diabetes Mellitus and its Prevention During Pandemic Period

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Abstract: The 2019 coronavirus (COVID-19) has caused public health concerns around the world. Diabetes is considered one of the highest risks and common comorbidities associated with higher mortality. The clinical manifestations of viral infections in pregnant women with diabetes mellitus are described. Coronavirus infections are considered a high risk condition for pregnant women, especially in the last trimester of pregnancy.

Key words: COVID-19, pregnant women with diabetes mellitus, blood glucose, pneumonia.

Relevance. Gestational diabetes mellitus (GDM) is the most common extragenital pathology of pregnancy and represents a serious medical and social problem, increasing the frequency of undesirable pregnancy outcomes for both the mother and the fetus. The history of the search for optimal criteria for glucose levels in pregnant women goes back about 60 years [3]. Today, the increase in the number of pregnant women with impaired carbohydrate metabolism has been reliably established [2]. This is due to both an increase in the incidence of diabetes in the population and changes in diagnostic criteria [1]. GDM is the most common cause of hyperglycemia in pregnant women encountered by endocrinologists and obstetricians-gynecologists [8,9]. Despite the achievements of obstetric diabetology, the overall incidence of pregnancy complications and newborn morbidity does not decrease [5,7]. In addition, GDM is a risk factor for the development of obesity, type 2 diabetes mellitus (T2DM) and cardiovascular diseases in the mother and offspring in the future [4,6].

An increase in the number of pregnant women with carbohydrate metabolism disorders is associated with a steady increase in the incidence of diabetes and obesity in the general population, which emphasizes the close pathogenetic connection of these pathologies [10,11]. The exact prevalence rate of GDM remains unknown and may vary significantly depending on the diagnostic criteria used for screening. According to various statistical data, the prevalence of GDM throughout the world ranges from 4 to 20% and has significant population differences [14,15]. Differences in epidemiological indicators may be due to the diversity of the populations studied. Thus, in countries with a low risk of developing GDM in pregnant women, such as Sweden, Australia, the USA (with the exception of Native Americans and some other population groups), the prevalence of this pathology is less than 2%, about 9.5% and 4.8%, respectively. According to domestic authors, in Uzbekistan, the frequency of GDM varies widely - from 1 to 12%, averaging about 7%, and significantly depends on diagnostic methods [12,13], the ethnic composition of the population, the prevalence of type 2 diabetes in

individual populations, economic conditions. It should be noted that 91.6% of cases of hyperglycemia during pregnancy are reported in low- and middle-income countries, where maternal health care is often limited [16].

Based on an analysis of studies in recent years, risk factors for the development of GDM also include:

1. polyhydramnios during pregnancy or in history;
2. large and inadequate weight gain during pregnancy and during each week of pregnancy;
3. premature birth, recurrent miscarriage (3 or more spontaneous miscarriages in the first and second trimesters or non-developing pregnancy) or a history of induced abortions;
4. history of preeclampsia ;
5. traumatic birth with concomitant neurological disorders in the child [21].

Factors of modern life, such as epidemics of obesity during childbearing age, physical inactivity, changes in eating habits (fast food), pregnancy in late reproductive age, multiple pregnancies, and the use of assisted reproductive technologies (ART), only aggravate the problem [18-39]. Possible reasons for the increased incidence of GDM after assisted reproductive technologies: the use of a gonadotropin- releasing hormone agonist (triptorelin acetate or diferilin) and estrogen preparations. In fetuses exposed to hyperglycemia during pregnancy, malformations and neonatal complications are more common, the percentage of birth injuries increases sharply, and in later life such children have a high risk of developing arterial hypertension, obesity, type 2 diabetes, the so-called metabolic programming [22].

Women with GDM are at high perinatal risk and require timely medical care [17]. Despite ongoing international controversy regarding which pregnant women need testing, whether “one-step” or “two-step” testing is optimal, and what glucose cutoff values should be used, the oral glucose tolerance test (OGTT) is still considered the gold standard for diagnosing GDM. However, in the current pandemic, both clinicians and pregnant women are increasingly refusing to perform OGTT. This is based on concerns regarding travel and time (up to 3 hours) spent in the potentially infectious environment of a health care setting. In addition, the diagnosis of GDM usually includes additional visits to consult an endocrinologist and conduct an ultrasound examination of the fetus, which introduces an additional risk of infection [20]. And as you know, in order to slow the spread of COVID-19, so-called social isolation is very important, including in medical institutions. During the COVID-19 pandemic, temporary changes to the recommended GDM screening algorithm during both pregnancy and the postpartum period are needed to reduce the number and duration of health care visits [19].

GDM is a heterogeneous syndrome. Data on the relationship between the height of a pregnant woman and the risk of developing GDM, obtained through meta-analysis, have been published. According to these data, an increase in the height of the subjects by 5 cm reduces the risk of developing GDM by 20%. In other words, the taller the patient, the lower the risk of developing GDM. A systematic review of the scientific literature concluded that GDM may influence epigenetic modifications in mother and offspring. However, larger studies are needed that include multiple cohorts of patients with GDM and their children. A randomized clinical trial (RCT) was conducted, based on the results of which it was concluded that metabolic syndrome 7 years after childbirth develops significantly more often in patients with fat metabolism disorders (FMD) and GDM than in patients without carbohydrate metabolism disorders.

Goal: Implementation of early screening methods based on biochemical and hormonal markers in the early diagnosis of GDM.

Material and methods of research. The choice of research methods used in the work was determined in accordance with industry standards for the scope of examination in obstetrics, recommendations for laboratory diagnostics of the carbohydrate metabolism system and statistical studies.

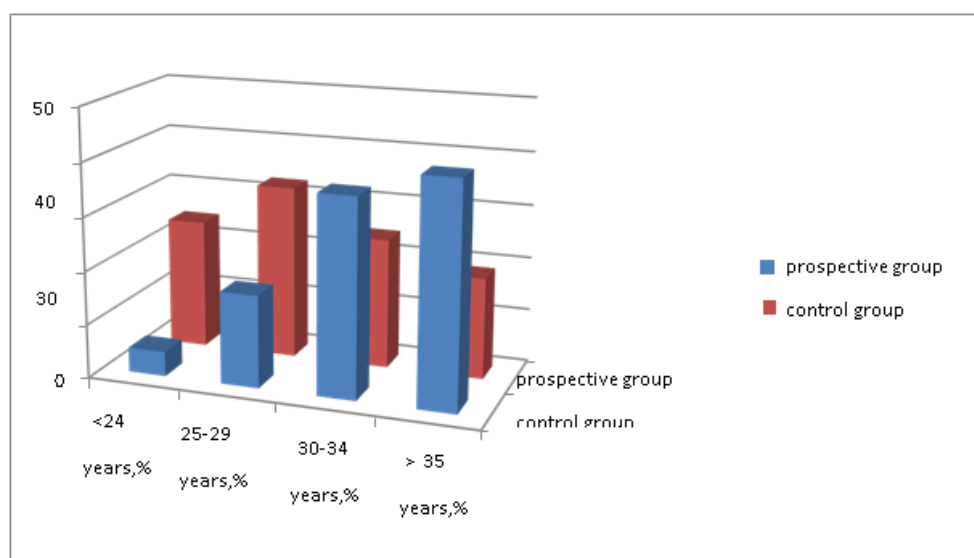
The retrospective group included 67 women who passed through the regional perinatal center of Bukhara and Navoi, the city maternity complex of Bukhara in the periods from 2017 to 2020. The main group consisted of prospectively 68 women whose pregnancy proceeded against the background of overt or gestational diabetes mellitus (GDM). The control group consisted of 36 women whose pregnancy proceeded physiologically. When managing pregnant women complicated by GDM, it is necessary to monitor hemodynamic parameters, maintain an observation sheet, complete blood count, urine test, fasting glucose, D- dimer (lactate dehydrogenase , C-reactive protein, leukocyte intoxication index, urinalysis, blood group and Rh affiliation, Ultrasound (anthropometry of the fetus), general condition of the woman in labor. It should be noted that out of 68 pregnant women, fasting glycosylated hemoglobin was checked in order to establish the duration of the process.

Biochemical studies included bilirubin, ALT and AST enzymes, total protein, urea and creatinine to determine the degree of liver and kidney dysfunction.

Of 68 pregnant women, only 26 received insulin from 6 to 10 units per day according to the recommendations of the endocrinologist.

Results and discussion : Some complications of pregnancy, being characteristic, are not only for GDM, which are more often observed in women with this particular disease. When studying the course of pregnancy and childbirth using birth histories and our own observations, it was revealed that all (87%) pregnant women with GDM had pregnancy and childbirth with some complications. And in most cases, several complications were observed in combination, both in the mother and in the fetus. Every second woman in the retrospective group had hypertensive pathologies.

PE and impaired functional state of the fetus are indications for delivery of pregnant women with GDM by cesarean section. As can be seen from our data, preeclampsia is observed in the retrospective group 56.7%, in the main group 75.4%, in the control group 18.3% against the background of previous vascular changes. Almost every second pregnant woman developed urinary tract infections: in the retrospective group 31.3%, in the main group 47.4%, in the control group 27.3%, which indicates a fairly wide prevalence of this pathology. Premature rupture of membranes in women in the retrospective group was observed in 41.8% of cases, in the main group in 54.4%, in the control group in 81.8% of cases.



In the control group, polyhydramnios was observed in 1 case (9%), which was confirmed by clinical signs and ultrasound data. Observing the postpartum period in groups of women with GDM, it was revealed that in 13 women (22.8% of cases) this period was complicated by early bleeding, which may have had a mixed etiology (atonic and coagulopathic origin); postpartum bleeding is also more often observed, which may be due to stretching of the uterus with polyhydramnios and large size of the fetus. Mostly, bleeding was observed in the first 2 hours after separation and delivery of the placenta and with a newborn body weight of more than 4000 grams during prolonged labor. Macrosomia with a fetal weight of more than 4500 grams is known to be the result of excess glucose supply to the fetus through the uteroplacental system. In our cases, macrosomia occurred in 56% of cases in the main group and in 27.3% of cases in the control group.

As is known, in newborns from mothers with diabetes, the risk of developing congenital anomalies increases by 3 times compared to the 1-2% baseline risk for all newborns. The most common defects are heart defects and developmental anomalies of the limbs. A typical but rather rare anomaly is sacral agenesis.

We analyzed the laboratory tests performed on pregnant women with GDM, general blood test, urine test, fasting glucose, fibrinogen, D- dimer.

It should be noted that out of 68 pregnant women, fasting glycosylated hemoglobin was checked in order to establish the duration of the process.

Indicators of laboratory data in pregnant women with GDM before and after childbirth in comparison with healthy ones

Name of analysis	Pregnant women with GDM before delivery (n =68)	Healthy pregnant women (n = 3 6)	Pregnant women with GDM after childbirth (n =68)	Healthy pregnant women (n = 3 6)
Hb (g/l)	91	96	90	92
Red blood cells (10 ¹² L)	2.8	3.1	2.9	3.0
Leukocytes (10 ⁹ L)	9.1	6.3	9.3	6.8
Platelets (10 ⁹ L)	225	298	265	289
ESR(mm/hour)	28	19	thirty	17
Total protein (g l)	63	69	62	67
Bilirubin (mmol/l)	18.9	11.9	16.9	12.3
ALT (mol/l)	0.9	0.5	0.8	0.5
AST (mol/l)	0.7	0.3	0.9	0.5
Urea (mmol/l)	8.8	5.6	9.1	4.9
Creatinine (mmol /l)	83	4.2	9.8	3.6
Fasting glucose (mol/l)	6.7	5.3	6.1	4.9
Glycated (HbA 1c)%	7.7	4.2	7.8	4.6
Homocysteine (mmol /l)	61.7	16.9 _	46.8	15, 2

As can be seen from the table, the general blood test indicators differ markedly in all parameters.

The hemoglobin content was significantly reduced in the group of pregnant women with GDM, amounting to 91 g/l, whereas in healthy women it was 96 g/l, which indicates that pregnant women with GDM are more susceptible to impaired oxygen supply, thereby being susceptible to reduced rates of adaptive reactions.

The indicators of erythrocytes are also low compared to the group of healthy women by 0.3, and all these data indicate that in the body of a pregnant woman, protective adaptive abilities are greater than in healthy pregnant women.

Analyzing the indicators of the white part of the blood, it should also be noted that inflammatory processes were more observed in the group of pregnant women with GDM, since diabetes mellitus in pregnant women is especially manifest in the 3rd trimester, which proves the high values of leukocytes and ESR in comparison with the group of healthy pregnant women. Elevated concentrations of leukocytes indicate a response of the whole organism to developing inflammation, which initially begins from local positions, with the transition to more generalized foci.

The leukocyte count averaged 9.1, while in the group of healthy pregnant women it was 2.8 ESR is also the most accessible method in maternity hospitals, and was also high in the main group at 9 mm/hour.

Procalcitonin and LII in 11 pregnant women were high, averaging 0.05 ng /ml, but did not reach values indicating generalization of infection (6 ng/ml on average), whereas in healthy people this figure was up to 2 ng /l.

Platelets, responsible for coagulation processes, which are important during childbirth and the postpartum period, were also lower than in the group of healthy pregnant women by 73 thousand, therefore, in the postpartum period, on the first day, 11 out of 68 pregnant women had bleeding.

Biochemistry data also differed in some indicators such as total protein, creatinine and urea, although they remained within normal limits on average.

Total protein, due to moderate anemia in the group of pregnant women with GDM, was 9 g/l lower, as well as creatinine and urea levels. Characteristics of kidney function were also changed. Indicators of urea and creatinine are 4.2 and 3.6 $\mu\text{mol / l}$ higher in the group with GDM than in healthy people, which also indicates impaired renal microcirculation, thereby excretory function.

Glycated hemoglobin, or glycohemoglobin (HbA1c), is a biochemical blood marker that reflects the average blood sugar level over a long period (three to four months), as opposed to blood glucose testing, which provides an idea of blood glucose levels only at the time of the test.

In our pregnant women with GDM, it averaged 7.7% before birth, which was within the normative data, but it should be noted that in healthy women this figure was significantly reduced by 3.2%.

The increase in glycohemoglobin in women closer to the end of labor, which coincided with our results. Due to the close deadlines, it was difficult for us to do anything and we were forced to adjust, as indicated above, the doses of administered insulin-containing drugs, with antioxidant therapy.

Clinically pregnant women suddenly began to feel dry mouth, frequent urge to urinate, and a tendency to periodic colds, especially in the cold season.

We were also able to promptly prescribe a strict diet for pregnant women and revise the insulin dose.

There were 2 negative cases when a pregnant woman did not follow a strict diet and mistakenly administered a small dose of insulin; within 24-36 hours, due to clinical manifestations, the level of glycohemoglobin and homocysteine increased simultaneously.

To provide a detailed description of the changes in the body in a pregnant woman with GDM, we examined the concentration of homocysteine in the blood for comparison in the two study groups. In the group with GSB, homocysteine was high at 19.3 $\mu\text{mol / l}$, while in the control group it was only 15.8 $\mu\text{mol / l}$.

A diagnostic marker such as homocysteine is formed in the body during the metabolism of the amino acid methionine. With low homocysteine levels in pregnant women, fetal development is considered normal. In the 1st and 2nd trimester of pregnancy it decreases and returns to normal after childbirth.

Thus, diabetes mellitus in pregnant women is a multifactorial disease. Diagnostics, especially accurate, which characterizes the true state of the pregnant woman herself, the course of gestation and intrauterine development of the fetus. The most reliable diagnostic tests for GDM are glycohemoglobin and homocysteine, which simultaneously increase when the course of the underlying disease is unfavorable, which is especially important when correcting the pathological condition.

We included all biochemical tests and fasting blood glucose as routine diagnostic methods, which can be checked in any medical institution.

Nutrition for pregnant women

Easily digestible carbohydrates are completely excluded from the diet (they are quickly absorbed from the intestines and increase blood glucose levels within 10-30 minutes after consumption):

- Sugar, fructose, jam, honey, caramel, candies, chocolate;
- Fruit juices (including juices provided in the antenatal clinic);
- Lemonades;
- Ice cream, pastries, cakes, condensed milk;
- Bakery products made from high-grade flour;
- Butter pastries (buns, buns, pies).

Foods with a high glycemic index are completely excluded from the diet.

The glycemic index (GI) is a measure of the effect of food on blood sugar levels. Each food is given a score from 0 to 100 depending on how quickly it raises your blood glucose levels. Glucose has a GI of 100, meaning it enters the bloodstream immediately, which is the benchmark against which other foods are compared.

Another indicator that helps predict how high your blood sugar level will rise after a meal and how long it will stay at this level is the glycemic load (GL). Calculated using the formula:

$$GL = [GI (\%) \times \text{amount of carbohydrates per serving (g)}] / 100$$

Glycemic load shows that eating foods with a low glycemic index but high amounts of carbohydrates will not be effective in maintaining normal post-meal blood sugar.

For example, let's compare the glycemic load of different foods:

Watermelon:

GI – 75, carbohydrates – 6.8 g per 100 g of product, $GL = (75 \times 6.8) / 100 = 6.6$ g.

Donuts:

GI – 76, carbohydrates – 38.8 g per 100 g of product, $GL = (76 \times 38.8) / 100 = 29.5$ g

Crumbled buckwheat:

GI – 50, carbohydrates – 30.6 g per 100 g of product, $GL = (50 \times 30.6) / 100 = 15.3$ g.

Pearl barley:

GI – 22, carbohydrates – 23 g per 100 product, $GL = (22 \times 23) / 100 = 5.1$ g.

Obviously, the glycemic load of foods increases as the amount of carbohydrates consumed and the glycemic index increase. Accordingly, it is possible to control the glycemic load by consuming low-GI foods in small portions several times a day.

Glycemic load scale:

During one meal

- Low up to 10 g;
- Average from 11 to 19 g;
- High – more than 20.

During the day

Low up to 80 g;

Average from 100 to 120 g;

High – more than 120.

It is necessary to give preference to foods with a medium and low glycemic load, consuming food in small portions, several times a day, excluding the intake of easily digestible carbohydrates.

It is necessary to exclude foods that have a high GI:

Sweet fruits and berries: grapes, bananas, persimmons, figs, cherries, melon, dates;

Vegetables: Potatoes, parsnips, pumpkin, boiled beets, boiled carrots, canned sweet corn and peas;

Porridges – millet, wheat grits, semolina, millet, polished varieties of rice, as well as all instant porridges;

- Homemade noodles, rice noodles;
- Milk;
- Varieties of white or black bread made from premium quality flour.

The most reliable method of preventing hypoglycemia is regular self-monitoring of glycemia.

Exercise for GDM

- ✓ walking ωNordic walking ωswimming
- ✓ running until the 3rd semester (if you ran before pregnancy)
- ✓ aerobics for pregnant women
- ✓ yoga for pregnant women
- ✓ regularity - daily 30-90 minutes o heart rate control : \uparrow heart rate (heart rate) by 50-70% of heart rate max o heart rate max = $(220 - \text{age}) : 2$
- ✓ Avoid exercises that increase blood pressure and cause uterine hypertonicity .

Preconception contraception.

Contraception in women with diabetes mellitus (DM) is challenging. More than half of women with diabetes do not use contraceptives at all, and among women who use them, ineffective methods were the most popular.

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region. Materials and methods. 80 pregnant women were examined at the gestation period from 8-36 weeks: 40 pregnant women with fetal growth restriction syndrome and 40 women with physiological pregnancy. The results of the study showed that the functionally unfavorable T allele and the association of polymorphism of the genotype C/T polymorphism of the ITGA2- α 2 gene is not a significant determinant of an increased risk of developing SORP in Uzbekistan ($\chi^2 < 3.8$, 10(1), 90).

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